

Gluconolacton 17.8 g and creatinine 5.7 g are dissolved in water 60 ml and propylene glycol 10 ml. More water is added to make a total volume of the solution to 100 ml. The pseudoamphoteric composition thus formulated has pH 3.2. The composition has pH 4.8 when 1 M instead of 0.5 M creatinine is incorporated into the formulation.

EXAMPLE 34

A pseudoamphoteric composition containing 1 M pyruvic acid and 1 M creatinine for dermatologic and cosmetic conditions may be formulated as follows.

2-Ketopropanoic acid (pyruvic acid) 8.8 g and creatinine 11.3 g are dissolved in water 25 ml. The solution thus obtained is mixed with sufficient amount of an oil-in-water emulsion to make a total volume of 100 ml. The amphoteric composition thus formulated has pH 3.4.

EXAMPLE 35

An amphoteric composition containing 0.5 M benzilic acid and 0.5 M L-lysine for cosmetic and dermatologic conditions may be formulated as follows.

2,2-Diphenyl 2-hydroxyethanoic acid (benzilic acid) 11.4 g and L-lysine 7.3 g are dissolved in water 40 ml and propylene glycol 20 ml. After all the crystals have been dissolved sufficient amount of ethanol is added to make a total volume of the solution to 100 ml. The amphoteric composition thus formulated has pH 4.9. The composition has pH 2.7 if no amphoteric compound is incorporated.

EXAMPLE 36

An amphoteric composition containing 0.5 M benzilic acid and 0.5 M L-histidine for cosmetic and dermatologic conditions may be formulated as follows.

Benzilic acid 11.4 g and L-histidine 7.8 g are dissolved in water 40 ml and propylene glycol 20 ml. Ethyl cellulose 2 g is added with stirring, and sufficient amount of ethanol is added to make a total volume of the gel to 100 ml. The amphoteric gel composition thus formulated has pH 5.0.

EXAMPLE 37

A pseudoamphoteric composition containing 0.5 M benzilic acid and 0.5 M creatinine for cosmetic and dermatologic conditions may be formulated as follows.

Benzilic acid 11.4 g and creatinine 5.7 g are dissolved in water 40 ml and propylene glycol 20 ml. Sufficient amount of ethanol is added to make a total volume of the solution to 100 ml. The amphoteric composition thus formulated has pH 4.9.

EXAMPLE 38

A pseudoamphoteric composition containing in combination 0.5 M 2-hydroxyethanoic acid and 0.05 % betamethasone dipropionate in a cream form for dermatologic disorders may be formulated as follows.

2-Hydroxyethanoic acid 3.8 g and creatinine 5.7 g are dissolved in 25 ml of water, and the solution thus obtained is mixed with 50 g of an oil-in-water emulsion. Betamethason dipropionate 1 % in ethanol solution 5 ml is added to the above mixture. More oil-in-water emulsion is added to make a total volume of 100 ml. The pseudoamphoteric composition thus formulated has pH 4.2.

EXAMPLE 39

A pseudoamphoteric composition containing in combination 0.5 M 2-hydroxyethanoic acid and 0.05% clobetasol propionate in a cream form for dermatologic disorders may be formulated as follows.

2-Hydroxyethanoic acid 3.8 g and creatinine 5.7 g are dissolved in 25 ml of water, and the solution thus obtained is mixed with 50 g of an oil-in-water emulsion. Clobetasol propionate 1 % in acetone solution 5 ml is added to the above mixture. More oil-in-water emulsion is added to make a total volume of 100 ml. The pseudoamphoteric composition thus formulated has pH 4.2.

EXAMPLE 40

A pseudoamphoteric composition containing in combination 0.5 M 2-hydroxyethanoic acid and 0.1% triamcinolone acetonide in a cream form for dermatologic disorders may be formulated as follows.

2-Hydroxyethanoic acid 3.8 g and creatinine 5.7 g are dissolved in 25 ml of water, and the solution thus obtained is mixed with 50 g of an oil-in-water emulsion. Triamcinolone acetonide 2% solution of acetone:ethanol (50:50), 5 ml is added to the above mixture. More oil-in-water emulsion is added to make a total volume of 100 ml. The pseudoamphoteric composition thus formulated has pH 4.2.

EXAMPLE 41

A pseudoamphoteric composition containing in combination 0.5 M 2-hydroxyethanoic acid and 0.2 % 5-fluorouracil in a cream form for dermatologic disorders may be formulated as follows.

2-Hydroxyethanoic acid 3.8 g and creatinine 5.7 g are dissolved in 20 ml of water, and the solution thus obtained is mixed with 50 g of an oil-in-water emulsion. 5-Fluorouracil 2% solution of propylene glycol: water (95:5), 10 ml is added to the above mixture. More oil-in-water emulsion is added to make a total volume of 100 ml. The pseudoamphoteric composition thus formulated has pH 4.1.

EXAMPLE 42

A pseudoamphoteric composition containing in combination 0.5 M 2-hydroxypropanoic acid and 0.05 % betamethasone dipropionate in a cream form for dermatologic disorders may be formulated as follows.

2-Hydroxypropanoic acid 4.5 g and creatinine 5.7 g are dissolved in 25 ml of water, and the solution thus obtained is mixed with 50 g of an oil-in-water emulsion. Betamethasone dipropionate 1% in ethanol solution 5 ml is added to the above mixture. More oil-in-water emulsion is added to make a total volume of 100 ml. The pseudoamphoteric composition thus formulated has pH 4.1.

EXAMPLE 43

A pseudoamphoteric composition containing in combination 0.5 M hydroxypropanoic acid and 0.05 % clobetasol propionate in a cream form for dermatologic disorders may be formulated as follows.

2-Hydroxypropanoic acid 4.5 g and creatinine 5.7 g are dissolved in 25 ml of water, and the solution thus obtained is mixed with 50 g of an oil-in-water emulsion. Clobetasol propionate 1% in acetone solution 5 ml is added to the above mixture. More oil-in-water emulsion is added to make a total volume of 100 ml. The pseudoamphoteric composition thus formulated has pH 4.1.

EXAMPLE 44

A pseudoamphoteric composition containing in combination 0.5 M 2-hydroxypropanoic acid and 0.1 % triamcinolone acetonide in a cream form for dermatologic disorders may be formulated as follows.

2-Hydroxypropanoic acid 4.5 g and creatinine 5.7 g are dissolved in 25 ml of water, and the solution thus obtained is mixed with 50 g of an oil-in-water emulsion. Triamcinolone acetonide 2% solution of acetone:ethanol (50:50), 5 ml is added to the above mixture. More oil-in-water emulsion is added to make a total volume of 100 ml. The pseudoamphoteric composition thus formulated has pH 4.1.

EXAMPLE 45

A pseudoamphoteric composition containing in combination 0.5 M 2-hydroxypropanoic acid and 0.2 % 5-fluorouracil in a cream form for dermatologic disorders may be formulated as follows.

2-Hydroxypropanoic acid 4.5 g and creatinine 5.7 g are dissolved in 20 ml of water, and the solution thus obtained is mixed with 50 g of an oil-in-water emulsion. 5-Fluorouracil 2% solution of propylene glycol:water (95:5), 10 ml is added to the above mixture. More oil-in-water emulsion is added to make a total volume of 100 ml. The pseudoamphoteric composition thus formulated has pH 4.1.

EXAMPLE 46

A pseudoamphoteric composition containing in combination 0.5 M 2-hydroxyethanoic acid and 2% clotrimazole in a cream form for athlete's foot and other fungal infections may be formulated as follows.

2-Hydroxyethanoic acid 3.8 g, clotrimazole 2 g and creatinine 5.7 g are dissolved in water 20 ml and propylene glycol 5 ml, and the solution thus obtained is mixed with enough amount of an oil-in-water emulsion to make a total volume of 100 ml. The pseudoamphoteric composition thus formulated has pH 4.2.

EXAMPLE 47

A pseudoamphoteric composition containing in combination 0.5 M 2-hydroxyethanoic acid and 2% erythromycin in solution form for acne may be formulated as follows.

2-Hydroxyethanoic acid 3.8 g, erythromycin 2 g and creatinine 5.7 g are dissolved in water 25 ml, ethanol 40 ml and propylene glycol 15 ml. More water is then added to make a total volume of 100 ml. The pseudoamphoteric composition thus formulated has pH 4.2.

EXAMPLE 48

A pseudoamphoteric composition containing in combination 0.5 M 2-hydroxyethanoic acid and 1 % ketoconazole in a cream form for fungal infections may be formulated as follows.

2-Hydroxyethanoic acid 3.8 g, ketoconazole 1 g and creatinine 5.7 g are dissolved in 25 ml of water, and the solution thus obtained is mixed with enough amount of an oil-in-water emulsion to make a total volume of 100 ml. The pseudoamphoteric composition thus formulated has pH 4.2.

EXAMPLE 49

A pseudoamphoteric composition containing in combination 0.5 M 2-hydroxypropanoic acid and 2% clotrimazole in a cream form for fungal infections may be formulated as follows.

2-Hydroxypropanoic acid 3.8 g, clotrimazole 2 g and creatinine 5.7 g are dissolved in 25 ml of water, and the solution thus obtained is mixed with enough amount of an oil-in-water emulsion to make a total volume of 100 ml. The pseudoamphoteric composition thus formulated has pH 4.1.

EXAMPLE 50

5 A pseudoamphoteric composition containing in combination 0.5 M 2-hydroxyethanoic acid and 2% tetracycline in a gel form for dermatologic disorders may be formulated as follows.

2-Hydroxyethanoic acid 3.8 g, tetracycline 2 g, creatinine 5.7 g, xanthan gum 0.2 g, carbomer-941 1 g, propylene glycol 5 ml, ethanol 20 ml and enough amount of water are homogenized to make a total volume of 100 ml. The pseudoamphoteric composition thus formulated for acne and oily skin has pH 4.2.

EXAMPLE 51

15 An amphoteric composition containing 0.2 M aleuritic acid and 0.1 M L-lysine in a solution form for cosmetic and dermatologic conditions may be formulated as follows.

Aleuritic acid 6.1 g and L-lysine 1.5 g are dissolved in sufficient amount of a solution from ethanol:propylene glycol 80:20 to make a total volume of 100 ml. The amphoteric composition thus formulated has pH 6.4.

EXAMPLE 52

25 A typical composition containing a dimeric form of alpha hydroxyacid in solution for acne, dandruff, and as a skin cleanser may be formulated as follows.

Glycolide powder 1.0 g is dissolved in ethanol 89 ml and propylene glycol 10 ml. The composition thus formulated has pH 4.0, and contains 1% active ingredient.

EXAMPLE 53

35 A typical composition containing a dimeric form of alpha hydroxyacid in ointment for dry skin, psoriasis, eczema, pruritus, wrinkles and other skin changes associated with aging may be formulated as follows.

Glycolide powder 2.0 g is mixed uniformly with petrolatum 66 g and mineral oil 32 g. The composition thus formulated contains 2% active ingredient.

EXAMPLE 54

40 A typical composition containing a full strength or a high concentration of an alpha hydroxyacid, alpha ketoacid or closely related compound for topical treatments of warts, keratoses, acne, age spots, nail infections, wrinkles and aging related skin changes may be prepared as follows.

45 If the alpha hydroxyacid, alpha ketoacid or closely related compound at full strength is a liquid form at room temperature such as 2-hydroxypropanoic acid, 2-ketopropanoic acid, methyl 2-ketopropanoate and ethyl 2-ketopropanoate, the compound is directly dispensed as 0.5 to 1 ml aliquots in small vials. If the compound is a solid form at room temperature such as 2-hydroxyethanoic acid and 2-methyl 2-hydroxypropanoic acid, it is first dissolved in minimal amount of an appropriate solvent or solvent system such as
50 water or ethanol and propylene glycol with or without a gelling agent. For example, 2-hydroxyethanoic acid 70 g is dissolved in water 30 ml, and the 70% strength 2-hydroxyethanoic acid thus obtained is dispensed as 0.5 to 1 ml aliquots in small vials. If a gelling agent is used, methyl cellulose or hydroxyethyl cellulose 1 g may be added to the above solution.

EXAMPLE 55

A typical composition containing an intermediate strength of an alpha hydroxyacid, alpha ketoacid or closely related compound for topical treatment of warts, keratoses, acne, nail infections, age spots, wrinkles and aging related skin changes may be prepared as follows.

2-Hydroxyethanoic acid or 2-ketopropanoic acid 40 g is dissolved in ethanol 54 g and propylene glycol 6 g, and the 40% strength solution thus obtained is dispensed as 5 to 10 ml aliquots in dropper bottles.

TEST RESULTS

In order to determine whether amphoteric and pseudoamphoteric compositions of the instant invention were therapeutically effective for various cosmetic conditions and dermatologic disorders, a total of more than 90 volunteers and patients participated in these studies. Some participating subjects were given two preparations; an amphoteric or pseudoamphoteric composition containing an alpha hydroxyacid or the related compound, and a vehicle placebo. Others were given multiple preparations containing a known pharmaceutical agent such as a corticosteroid with or without incorporation of an amphoteric or pseudoamphoteric composition consisting of an alpha hydroxyacid or the related compound of the instant invention. The amphoteric and pseudoamphoteric compositions were formulated according to the Examples described in the previous section.

1. Common dry skin.

Human subjects having ordinary dry skin or with moderate degrees of dry skin as evidenced by dryness, flaking and cracking of the skin were instructed to apply topically the lotion, cream or ointment containing an alpha hydroxyacid or the related compound in amphoteric or pseudoamphoteric composition, on the affected area of the skin. Topical application, two to three times daily, was continued for two to four weeks.

In all the 28 subjects tested, the feeling of the skin dryness disappeared within a week of topical application. The rough and cracked skin became less pronounced and the skin appeared normal and felt smooth after several days of topical treatment. The alpha hydroxyacids and the related compounds which have been found to be therapeutically effective when incorporated into the amphoteric or pseudoamphoteric compositions for dry skin are as follows:

2-hydroxyethanoic acid (glycolic acid), 2-hydroxypropanoic acid (lactic acid), 2-methyl-2-hydroxypropanoic acid (methylactic acid), phenyl 2-hydroxyethanoic acid (mandelic acid), phenyl 2-methyl-2-hydroxyethanoic acid (atrolactic acid), 3-phenyl-2-hydroxypropanoic acid (phenyllactic acid), diphenyl 2-hydroxyethanoic acid (benzilic acid), gluconolactone, tartaric acid, citric acid, saccharic acid, malic acid, tropic acid, glucuronic acid, galacturonic acid, gluconic acid, 3-hydroxybutanoic acid, quinic acid, ribonolactone, glucuronolactone, galactonolactone, pyruvic acid, methyl pyruvate, ethyl pyruvate, phenylpyruvic acid, benzoylformic acid and methyl benzoylformate.

The ordinary dry skin conditions, once restored to normal appearing skin, remained improved for some time until causes of dry skin, such as low humidity, cold weather, excessive contact pressure, detergents, soaps, solvents, chemicals, etc., again caused recurrence of the dry skin condition. On continued use it was also found that twice daily topical application of an amphoteric or pseudoamphoteric composition containing an alpha hydroxyacid or the related compound of the instant invention prevented the development of new dry skin lesions.

2. Severe dry skin.

In severe dry skin, the skin lesions are different from the ordinary dry skin. A main cause of severe dry skin is inherited genetic defects of the skin. The involved skin is hypoplastic, fissured and has thick adherent scales. The degree of thickening is such that lesions are palpably and visually elevated. The thickened adherent scales cause the surface of involved skin to be markedly rough and uneven. These two attributes of thickness and texture can be quantified to allow objective measurement of degree of improvement from topically applied test materials as follows:

DEGREE OF IMPROVEMENT					
	None	Mild	Moderate	Substantial	Complete
	(0)	(1+)	(2+)	(3+)	(4+)
Thickness	Highly elevated	Detectable reduction	Readily apparent reduction	Barely elevated	Normal thickness
Texture	Visibly rough	Palpably rough	Uneven but not rough	Slightly uneven	Visibly and palpably smooth

By means of such parameters, degrees of change in lesions can be numerically recorded and comparisons made of one treated site to another.

In order to evaluate the amphoteric and pseudoamphoteric compositions of the instant invention, a total of 6 patients having severe dry skin conditions were treated with the compositions containing an alpha hydroxyacid or the related compound.

Tested areas were of a size convenient for topical applications, i.e., circles 5 cm in diameter demarcated with a plastic ring of that size inked on a stamp pad. The medicinal lotions or creams were topically applied by the patient in an amount sufficient to cover the treatment sites. Applications were made three times daily and without occlusive dressings. Applications were discontinued at any time when resolution of the lesion on the treatment area was clinically judged to be complete.

The test results of amphoteric and pseudoamphoteric compositions containing the following alpha hydroxyacids or the related compounds on patients with severe dry skin are summarized as follows:

4+ Effectiveness; glycolic acid, lactic acid, methylactic acid, mandelic acid, tropic acid, atrolactic acid and pyruvic acid.

3+ Effectiveness; benzilic acid, gluconolactone, malic acid, tartaric acid, citric acid, saccharic acid, methyl pyruvate, ethyl pyruvate, phenyllactic acid, phenylpyruvic acid, glucuronic acid and 3-hydroxybutanoic acid.

2+ Effectiveness; mucic acid, ribonolactone, 2-hydroxydodecanoic acid, quinic acid, benzoylformic acid and methyl benzoylformate.

3. Psoriasis.

The involved skin in psoriasis is hyperplastic (thickened), erythematous (red or inflamed), and has thick adherent scales. The degree of thickening is such that lesions are elevated up to 1 mm above the surface of adjacent normal skin; erythema is usually an intense red; the thickened adherent scales cause the surface of involved skin to be markedly rough and uneven. These three attributes of thickness, color and texture can be quantified to allow objective measurement of degree of improvement from topically applied test materials as follows.

DEGREE OF IMPROVEMENT					
	None	Mild	Moderate	Substantial	Complete
	(0)	(1+)	(2+)	(3+)	(4+)
THICKNESS	Highly elevated	Detectable reduction	Readily apparent reduction	Barely elevated	Normal thickness
TEXTURE	Visibly rough	Palpably rough	Uneven but not rough	Slightly uneven	Visibly and palpably smooth
COLOR	Intense Red	Red	Dark Pink	Light Pink	Normal Skin Color

By means of such parameters, degree of improvement in psoriatic lesions can be numerically recorded and comparisons made of one treated site to another.

Patients having psoriasis participated in this study. Amphoteric and pseudoamphoteric compositions containing both an alpha hydroxyacid or the related compound and a corticosteroid were prepared according to the Examples. Compositions containing only a corticosteroid were also prepared and included in the comparison test. Test areas were kept to minimal size convenient for topical application, i.e., circles approximately 4 cm in diameter. The medicinal compositions were topically applied by the patient in an amount (usually about 0.1 milliliter) sufficient to cover the test site. Applications were made two to three times daily and without occlusive dressings. Test periods usually lasted for two to four weeks. The test results on patients having psoriasis are summarized on the following table.

Topical Effects on Psoriasis of Antipsoriatic Compositions

Compositions*

Therapeutic
Effectiveness

Hydrocortisone 2.5% alone

1+

With lactic acid

2+

With glycolic acid

2+

 Compositions*

 Therapeutic
Effectiveness

5	With ethyl pyruvate	2+
	With methyl pyruvate	2+
10	With benzilic acid	2+
	With pyruvic acid	2+
	With methyllactic acid	2+
15	Hydrocortisone 17-valerate 0.2% alone	2+
	With lactic acid	3+
20	With glycolic acid	3+
	With benzilic acid	3+
	With ethyl pyruvate	3+
25	With methyl pyruvate	3+
	With gluconolactone	3+
30	With pyruvic acid	3+
	Betamethasone dipropionate 0.05% alone	3+
	With lactic acid	4+
35	With glycolic acid	4+
	With ethyl pyruvate	4+
40	With methyl pyruvate	4+
	With mandelic acid	4+
	With benzilic acid	4+
45	Clobetasol propionate 0.05% alone	3+
	With lactic acid	4+
50	With glycolic acid	4+

 Compositions*

 Therapeutic
Effectiveness

5	With ethyl pyruvate	4+
	With methyl pyruvate	4+
10	With methyllactic acid	4+
	With mandelic acid	4+
	With tropic acid	4+
15	With benzilic acid	4+

20 * Except the "alone" preparations, all others were
amphoteric or pseudoamphoteric compositions containing
0.2 to 2M alpha hydroxyacids or related compounds.

25 We have also found that an amphoteric or pseudoamphoteric composition containing an alpha
hydroxyacid or the related compound in combination with an antimetabolite agent such as 5-fluorouracil with
or without additional incorporation of a corticosteroid is therapeutically effective for topical treatment of
30 psoriasis.

4. Eczema.

35 In a topical treatment of eczema patients, hydrocortisone alone at 2.5% or hydrocortisone 17-valerate
alone at 0.2% would achieve only 2+ improvement, and betamethasone dipropionate or clobetasol
propionate alone at 0.05% would achieve only a 3+ improvement on all the eczema patients tested. Test
results of amphoteric and pseudoamphoteric compositions containing both a corticosteroid and one of the
following alpha hydroxyacids or the related compounds are shown as follows:

40 3+ Effectiveness; hydrocortisone 2.5% or hydrocortisone 17-valerate 0.2% plus lactic acid, glycolic acid,
mandelic acid, ethyl pyruvate, gluconolactone, benzilic acid or ribonolactone.

4+ Effectiveness; betamethasone dipropionate or clobetasol propionate 0.05% plus lactic acid, glycolic
acid, mandelic acid, ethyl pyruvate, methyl pyruvate, benzilic acid, gluconolactone, citric acid, tartaric acid
or methyllactic acid.

5. Oily Skin and Skin Cleanse.

50 Human subjects having oily skin or blemished skin as well as acne patients having extremely oily skin
participated in this study. Amphoteric and pseudoamphoteric compositions containing alpha hydroxyacids
r the related compounds were formulated in solution or gel form.

Each participating subject received a solution or a gel preparation containing an alpha hydroxyacid or a
related compound in an amphoteric or pseudoamphoteric composition. The participating subjects were
instructed to apply topically the solution or gel medication on the affected areas of forehead or other part of
55 the face. Three times daily applications were continued for 2 to 6 weeks.

The degree of improvement of oily skin as well as the rate of improvement of acne lesions were
clinically evaluated. Most participants reported that oiliness of skin disappeared within one to two weeks of
topical administration, and the skin so treated became smooth and soft. Many participating subjects

preferred gel preparations than solution compositions. It was found that all the participants showed substantial improvements on oily skin and acne lesions by six weeks of topical administration of amphoteric or pseudoamphoteric compositions containing alpha hydroxyacids or the related compounds of the instant invention.

Those alpha hydroxyacids and the related compounds which have been found to be therapeutically effective for oily skin and as skin cleansers include: benzoic acid, glycolic acid, lactic acid, methylactic acid, mandelic acid, pyruvic acid, ethyl pyruvate, methyl pyruvate, tropic acid, malic acid, gluconolactone, 3-hydroxybutanoic acid, glycolide and polyglycolic acid. As a skin cleanser for oily skin or acne-prone skin, the amphoteric or pseudoamphoteric composition containing an alpha hydroxyacid or the related compound may also be incorporated with other dermatologic agents. For example, an amphoteric gel composition may consist of both an alpha hydroxyacid and erythromycin or tetracycline.

6. Acne

Amphoteric and pseudoamphoteric compositions containing alpha hydroxyacids or the related compounds of the instant invention in a solution or gel form were provided to patients having comedogenic and/or papulopustular lesions of acne. Each participating patient was instructed to apply topically the composition on the involved areas of the skin such as forehead, face and chest. Three times daily administration was continued for 6 to 12 weeks.

The degree and rate of improvement on acne lesions were clinically evaluated. It was found that acne lesions consisting mainly of comedones improved substantially after 6 to 8 weeks of topical administration with the amphoteric or the pseudoamphoteric composition containing an alpha hydroxyacid or the related compound. The time for complete clearing of comedogenic acne treated with the amphoteric or pseudoamphoteric composition of the instant invention varied from 6 to 12 weeks.

As a topical treatment for papulopustular and/or pustular acne the amphoteric or pseudoamphoteric composition containing an alpha hydroxyacid or the related compound may incorporate in addition an antiacne agent. The antiacne agents include antibiotics such as erythromycin, tetracycline, clindamycin, meclocycline and minocycline, and retinoids such as retinoic acid. Such combination compositions have been found to be therapeutically more effective for topical treatment of severe acne.

7. Age Spots

Many small and large discolored lesions, commonly called age spots on the face and the back of the hands are benign keratoses, if they are not variants of actinic keratoses. Very few of such age spots are true lentigines, therefore alpha hydroxyacids and the related compounds may be effective in eradicating most age spots without concurrent use of skin bleaching agents such as hydroquinone and monobenzone. However, additional beneficial effects have been found when a skin bleaching agent such as hydroquinone or monobenzone is also incorporated into the compositions of the instant invention for age spots involving pigmented lesions.

Amphoteric and pseudoamphoteric compositions containing alpha hydroxyacids or the related compounds, with or without incorporation of hydroquinone were provided to volunteer subjects and patients having age spot keratoses, melasma, lentigines and/or other pigmented lesions. Each participating subject received two products, i.e., with or without the addition of 2% hydroquinone to the amphoteric or pseudoamphoteric composition containing an alpha hydroxyacid or the related compound.

The volunteer subjects and patients were instructed to apply topically one medication on one side of the body such as left side of the face or on the back of the left hand, and the other medication on the other side of the body such as on right side of the face or on the back of the right hand. Specific instructions were given to the participating subjects that the medications were applied three times daily to the lesions of age spot keratoses, melasmas, lentigines and/or other pigmented lesions. Clinical photos were taken of participating subjects before the initiation of the topical treatment and every 4 weeks during the course of treatment.

At the end of 4 to 8 weeks, improvement of age spot keratoses was clinically discernible. After 4 to 6 months of topical treatment, substantial improvement of age spot keratoses occurred in the majority of subjects tested. Complete eradication of age spot keratoses occurred after 6 to 9 months of topical administration with the amphoteric or pseudoamphoteric compositions of the instant inventions.

Amphoteric or pseudoamphoteric compositions containing both an alpha hydroxyacid or the related

compound and hydroquinone were judged to be more effective in eradicating pigmented age spots, melasma, lentigines and other pigmented lesions.

The alpha hydroxyacids and the related compounds which have been found to be therapeutically effective for age spots with or without combination with hydroquinone include glycolic acid, lactic acid, methylactic acid, mandelic acid, pyruvic acid, methyl pyruvate, ethyl pyruvate, benzilic acid, gluconolactone, malic acid, tartaric acid, citric acid and tropic acid. For flat or slightly elevated seborrheic keratoses on the face and/or the back of the body, amphoteric or pseudoamphoteric compositions containing higher concentrations of alpha hydroxyacids or the related compounds have been found to be effective in eradicating such lesions.

Actinic keratoses may be successfully treated with amphoteric or pseudoamphoteric compositions containing alpha hydroxyacids or the related compounds in combination with an antimetabolite agent such as 5-fluorouracil.

8. Warts.

Eradications of common warts by topical application of amphoteric or pseudoamphoteric compositions require higher than usual concentrations of alpha hydroxyacids or the related compounds in the formulations. The amphoteric or pseudoamphoteric compositions were formulated as a liquid or light gel form, and dispensed usually as 0.5-1 ml aliquots in small vials.

Topical applications were made discreetly to wart lesions by adult patients or by responsible adult family members. For ordinary usual warts of hands, fingers, palms and soles topical applications were made 2 to 4 times daily, and were continued for 2 to 6 weeks. Generally, the overlying stratum corneum of the wart lesion change in appearance after several weeks topical application of the composition. In most cases, the wart lesion simply fell off. The skin then healed normally without forming any scars.

We have also found that when a dermatologic agent such as 5-fluorouracil is incorporated into the amphoteric or pseudoamphoteric compositions containing alpha hydroxyacids or the related compounds, the medications have been very effective for topical treatment of warts without using higher concentrations of alpha hydroxyacids or the related compounds.

The alpha hydroxyacids and the related compounds which have been found to be therapeutically effective for topical treatment of warts with or without incorporation of 5-fluorouracil include glycolic acid, lactic acid, pyruvic acid, ethyl pyruvate, methyl pyruvate and mandelic acid.

Topical formulations and compositions containing specific alpha hydroxyacids, alpha ketoacids or the related compounds at full strengths or high to intermediate concentrations prepared according to Examples 54 and 55, without utilizing amphoteric or pseudoamphoteric systems, have also been tested for ordinary warts of the hands, fingers, palms and soles. Participating patients have been advised to apply a small drop of the medication with a toothpick or a fine caliber brush to the center of a wart lesion only. Prescribed applications have been 3 to 6 times daily, and are continued until the patient feels pain.

For the more rough-surfaced wart, the duration of application has been as short as one or a few days. For lesions with more compact, less permeable stratum corneum, the time to experience gain has been longer. Frequency and duration of applications have been modified according to other clinical responses and reactions of lesions, and the patient or responsible family member is instructed accordingly.

For example, some clinical manifestations other than pain have also been used as a signal to interrupt application. These manifestations have included distinct blanching of the lesions or distinct peripheral erythema. Very often, discomfort is the usual signal of clinical reactions.

Generally, the overlying stratum corneum of the wart lesions became loose, and the whole wart lesion simply fell off. The skin then healed normally without forming any scars.

9. Athlete's Foot and Nail Infections

Amphoteric and pseudoamphoteric compositions containing both an antifungal agent and one of the alpha hydroxyacids or the related compounds were provided to patients having frequent recurrence of fungal infections involving the foot. The antifungal agents include clotrimazole, miconazole, ketoconazole and griseofulvin. When both feet but not toe nails were involved in the infection, the patients were instructed to apply topically the compositions of the instant invention on the left foot, and a brand-name antifungal product on the right foot. Three times daily applications were continued for one to four weeks. The degree and rate of improvement on skin lesions were clinically evaluated, and comparison was made on side of

the body against the other. It was found that the skin lesions improved much faster with the amphoteric or pseudoamphoteric compositions containing both the antifungal agent and the alpha hydroxyacid or the related compound. The alpha hydroxyacids or the related compounds seemed to enhance the efficacies of the antifungal agents, and also to eliminate the discomforts such as itching, tingling, burning and irritation due to fungal infections. When toe nails were not involved the infected skin generally healed within one to two weeks from topical application of the amphoteric or pseudoamphoteric composition containing both an antifungal agent and an alpha hydroxyacid or the related compound.

Fungal infections of the nails are very difficult to treat, because antifungal products to date are not therapeutically effective for topical treatment of nails. One of the reasons is that most antifungal drugs have not been formulated as bioavailable forms in the commercial products. When tow nails were involved in the infections, patients were provided with amphoteric or pseudoamphoteric compositions containing in combination an antifungal agent and an alpha hydro xyacid or an alpha ketoacid at higher concentrations ranging from 20 to 99%, dispensed as 1-2 ml aliquots in small vials. The patients were instructed to apply topically the compositions discreetly to the infected nail surface by means of a fine calibre paint brush. the technique was the same as for application of nail polish, that is careful avoidance of contact with lateral nail folds or any peri-ungual skin. Once or twice daily applications were continued for 2 to 8 weeks.

As mentioned above, while brand-name antifungal products are usually not effective against fungus infections within or underneath the nail, it was found that the amphoteric or pseudoamphoteric compositions containing an antifungal agent and an alpha hydroxyacid or alpha ketoacid were therapeutically effective in eradicating fungal infections of the nails. Such treatment may cause in some instances the treated nail plate to become loose and eventually fell off from the nail bed. This happened quite naturally without any feeling of pain nor bleeding, and the skin lesion healed quickly with normal growth of a new nail.

10. Wrinkles

Wrinkles of skin may be due to natural aging and/or sun damage. Most fine wrinkles on the face are due to natural or innate aging; while coarse wrinkles on the face are the consequence of actinic or sun damage. Although the real mechanism of wrinkles formation in the skin is still unknown, it has been shown that visible fine wrinkles are due to diminution in the number and diameter of elastic fibers in the papillary dermis, and also due to atrophy of dermis as well as reduction in subcutaneous adipose tissue. Histopathology and electron microscopy studies indicate that coarse wrinkles are due to excessive deposition of abnormal elastic materials in the upper dermis and thickening of the skin. At present there are n commercial products which have been found to be therapeutically effective for topical eradication of wrinkles, although retinoic acid (tretinoin) has been shown to be beneficial for sun damaged skin.

In order to determine whether the amphoteric or pseudoamphoteric composition containing the alpha hydroxyacids, alpha ketoacids or the related compounds are therapeutically effective for wrinkles, patients and volunteer subjects participated in this study. The participants were instructed to apply the formulations of the instant invention twice daily on areas of facial wrinkles for 4 to 12 months. All participants were told to avoid sun exposure, and to use sunscreen products if exposure to sunlight was unavoidable. Photographs of each side of the face for each participant were taken at the beginning of the study and repeated at one to three-month intervals. The participants were asked not to wear any facial make-up at the time of each office visit. Standardized photographic conditions were used including the use of same lot of photographic film, the same light source at two feet from the face, aimed at a locus on the frontal aspect of each cheek. Each time photographs were taken with camera aimed perpendicular to the cheek. At the end of study twenty two participants had been entered into the study for at least four months. Clinical evaluations and review of photographs have revealed substantial reductions in facial wrinkles of the temporal region and cheek area on at least one side of the face in eighteen cases. Degree of improvement and reduction in wrinkles has been evaluated and determined to be mild to moderate in six participants but very substantial in twelve participants.

The alpha hydroxyacids, alpha ketoacids and other related compounds including their lactone forms which may be incorporated into the amphoteric and pseudoamphoteric compositions for cosmetic conditions and dermatologic disorders such as dry skin, acne, age spots, keratoses, warts and skin wrinkl s r in combination with other dermatologic agents to enhance therapeutic effects includ the following:

(1) Alkyl Alpha Hydroxyacids

2-Hydroxyethanoic acid (Glycolic acid), 2-Hydroxypropanoic acid (Lactic acid), 2-Methyl 2-hydroxypropanoic acid (Methyl lactic acid), 2-Hydroxybutanoic acid, 2-Hydroxypentanoic acid, 2-Hydroxyhexanoic acid, 2-Hydroxyheptanoic acid, 2-Hydroxyoctanoic acid, 2-Hydroxynonanoic acid, 2-Hydroxydecanoic acid, 2-Hydroxyundecanoic acid, 2-Hydroxydodecanoic acid (Alpha hydroxylauric acid), 2-Hydroxytetradecanoic acid (Alpha hydroxymyristic acid), 2-Hydroxyhexadecanoic acid (Alpha hydroxypalmitic acid), 2-Hydroxyoctadecanoic acid (Alpha hydroxystearic acid), 2-Hydroxyeicosanoic acid (Alpha hydroxyarachidonic acid).

(2) Alkyl And Aryl Alpha Hydroxyacids

2-Phenyl 2-hydroxyethanoic acid (Mandellic acid), 2,2-Diphenyl 2-hydroxyethanoic acid (Benzilic acid), 3-Phenyl 2-hydroxypropanoic acid (Phenyllactic acid), 2-Phenyl 2-methyl 2-hydroxyethanoic acid (Atrolactic acid), 2-(4'-Hydroxyphenyl) 2-hydroxyethanoic acid, 2-(4'-Chlorophenyl) 2-hydroxyethanoic acid, 2-(3'-Hydroxy-4'-methoxyphenyl) 2-hydroxyethanoic acid, 2-(4'-Hydroxy-3'-methoxyphenyl) 2-hydroxyethanoic acid, 3-(2'-Hydroxyphenyl) 2-hydroxypropanoic acid, 3-(4'-Hydroxyphenyl) 2-hydroxypropanoic acid, 2-(3',4'-Dihydroxyphenyl) 2-hydroxyethanoic acid.

(3) Polyhydroxy Alpha Hydroxyacids

2,3-Dihydroxypropanoic acid (Glyceric acid), 2,3,4-Trihydroxybutanoic acid (Isomers; erythronic acid, threonic acid), 2,3,4,5-Tetrahydroxypentanoic acid (Isomers; ribonic acid, arabinonic acid, xylonic acid, lyxonic acid), 2,3,4,5,6-Pentahydroxyhexanoic acid (Isomers; aldonic acid, altronic acid, gluconic acid, mannoic acid, gulonic acid, Idonic acid, galactonic acid, talonic acid), 2,3,4,5,6,7-Hexahydroxyheptanoic acid (Isomers; glucoheptonic acid, galactoheptonic acid, etc.)

(4) Polycarboxylic Alpha Hydroxyacids

2-Hydroxypropane 1,3-dioic acid (Tartronic acid), 2-Hydroxybutane-1,4-dioic acid (Malic acid), 2,3-Dihydroxybutane-1,4-dioic acid (Tartaric acid), 2-Hydroxy-2-carboxypentane-1,5-dioic acid (Citric acid), 2,3,4,5-Tetrahydroxyhexane-1,6-dioic acid (Isomers; saccharic acid, mucic acid, etc.)

(5) Alpha Hydroxyacid Related Compounds

Ascorbic acid, quinic acid, isocitric acid, tropic acid, 3-chlorolactic acid, trethocanic acid, cerebronic acid, citramalic acid, agaricic acid, 2-hydroxynervonic acid and aleuritic acid.

(6) Alpha Ketoacids And Related Compounds

2-Ketoethanoic acid (Glyoxylic acid), Methyl 2-ketoethanoate, 2-Ketopropanoic acid (Pyruvic acid), Methyl 2-ketopropanoate (Methyl pyruvate), Ethyl, 2-ketopropanoate (Ethyl pyruvate), Propyl 2-ketopropanoate (Propyl pyruvate), 2-Phenyl-2-ketoethanoic acid (Benzoylformic acid), Methyl 2-phenyl-2-ketoethanoate (Methyl benzoylformate), Ethyl 2-phenyl-2-ketoethanoate (Ethyl benzoylformate), 3-Phenyl-2-ketopropanoic acid (Phenylpyruvic acid), Methyl 3-phenyl-2-ketopropanoate (Ethyl phenylpyruvate), 2-Ketobutanoic acid, 2-Ketopentanoic acid, 2-Ketohexanoic acid, 2-Ketoheptanoic acid, 2-Ketooctanoic acid, 2-Ketododecanoic acid, Methyl 2-ketooctanoate

The amphoteric and pseudoamphoteric compounds which may be incorporated into the compositions of the instant invention for cosmetic and dermatologic conditions include amino acids, peptides, polypeptides, proteins and the like compounds such as creatinine and creatine.

The dimeric and polymeric forms of alpha hydroxyacids and the related compounds which may be incorporated into the compositions of the instant invention include acyclic esters and cyclic ester; for example, glycolyl glycollate, lactyl lactate, glycolide, lactide, polyglycolic acid and polylactic acid.

Claims

1. A pharmaceutical or cosmetic composition comprising in combination an amphoteric or pseudoamphoteric agent and an alpha hydroxyacid, an alpha ketoacid or a related compound in a pharmaceutically acceptable vehicle for topical application.
- 5 2. A composition comprising a cosmetic or pharmaceutical agent in an amphoteric or pseudoamphoteric system comprising an alpha hydroxyacid, an alpha ketoacid or a related compound in a pharmaceutically acceptable vehicle for topical treatment of cosmetic conditions or medical disorders.
3. A composition according to claim 2 wherein said cosmetic or pharmaceutical agent is selected from agents that improve or eradicate age spots; keratoses and wrinkles; analgesics; anaesthetics; antiacne
10 agents; antibacterials; antiyeast agents; antifungal agents; antiviral agents; antidandruff agents; antidermatitis agents; antipruritic agents; antiemetics; antimotionsickness agents; antiinflammatory agents; antihypertensive agents; antidyshidrotic agents; antiperspirants; antipsoriatic agents; antiseborrheic agents; hair conditioners and hair treatment agents; antiaging and antiwrinkle agents; antiasthmatic agents and bronchodilators; sunscreen agents; antihistamine agents; skin lightening agents; depigmenting agents; vitamins;
15 corticosteroids; tanning agents; hormones; retinoids; topical cardiovascular agents or dermatologicals.
4. A composition according to claim 2 wherein said cosmetic or pharmaceutical agent is selected from clotrimazole, ketoconazole, miconazole, griseofulvin, hydroxyzine, diphenhydramine, pramoxine, lidocaine, procaine, mepivacaine, hydroquinone, monobenzone, erythromycin, tetracycline, clindamycin, meclocycline, minocycline, naproxen, ibuprofen, theophylline, cromolyn, albuterol, retinoic acid, 13-cis retinoic acid,
20 hydrocortisone, hydrocortisone 21-acetate, hydrocortisone 17-valerate, hydrocortisone 17-butyrate, betamethasone dipropionate, triamcinolone acetonide, fluciclonide, clobetasol propionate, benzoyl peroxide, crotamiton, propranolol, promethazine, vitamin A palmitate or vitamin E acetate.
5. A composition according to any preceding claim which includes an amphoteric or pseudoamphoteric agent selected from amino acids, dipeptides, polypeptides, proteins, imidazoline derivatives, lecithin
25 derivatives, related agents or metallic oxides.
6. A composition according to any preceding claim which includes an amphoteric or pseudoamphoteric agent selected from glycine, alanine, valine, leucine, isoleucine, serine, threonine, cysteine, cystine, methionine, aspartic acid, asparagine, glutamic acid, glutamine, arginine, lysine, 5-hydroxylysine, histidine, phenylalanine, tyrosine, tryptophan, 3-hydroxyproline, 4-hydroxyproline, proline, homocysteine, homocystine,
30 homoserine, ornithine, citrulline, creatine, creatinine, 3-aminopropanoic acid, 2-aminobutanoic acid, 4-aminobutanoic acid, 2-amino-2-methylpropanoic acid, 2-methyl-3-aminopropanoic acid, theanine, phenylglycine, canavanine, canaline, 4-hydroxyarginine, 4-hydroxyornithine, homoarginine, 4-hydroxyhomoarginine, β -lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropanoic acid, 2,6-diaminopimelic acid, 2-amino-3-phenylbutanoic acid, 2-methylserine, 3-phenylserine, betaine, taurine, cysteinesulfinic acid, methionine sulfoxide, methionine sulfone, 3,5-diiodotyrosine, thyroxine, monoiodotyrosine, pipercolic acid, 4-aminopipercolic acid,
35 4-methylproline, glycylglycine, carnosine, anserine, ophidine, homocarnosine, β -alanyllysine, β -alanylarginine, glutathione, ophthalmic acid, norophthalmic acid, bradykinin, glucagon, protamines, histone, cocoamphoglycine, cocoamphopropionate, cocamphopropylsulfonate, phosphatidyl ethanolamine, phosphatidyl serine, sphingomyelin, stearamidoethyl, diethylamine, stearamidoethyl diethanolamine, stearamidopropyl dimethylamine, quaternary ammonium hydroxide, quaternium hydroxide, aluminum oxide or zinc oxide.
7. A composition according to any preceding claim wherein said alpha hydroxyacid is selected from alkyl alpha hydroxyacids, aralkyl and aryl alpha hydroxyacids, polyhydroxy alpha hydroxyacids and polycarboxylic alpha hydroxyacids having the following chemical formula:
45 (Ra) (Rb) C (OH) COOH
wherein Ra and Rb are H, F, Cl, Br, alkyl, aralkyl or aryl group of saturated or unsaturated, isomeric or non-isomeric, straight or branched chain or cyclic form, having 1 to 25 carbon atoms, and in addition Ra and Rb may carry OH, CHO, COOH and alkoxy group having 1 to 9 carbon atoms, said alpha hydroxyacid existing as a free acid or lactone form, or in salt form with an organic base or an inorganic alkali, and as stereoisomers as D, L, and DL forms when Ra and Rb are not identical.
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8. A composition according to claim 7 wherein said alkyl alpha hydroxyacid is selected from 2-Hydroxyethanoic acid (Glycolic acid), 2-Hydroxypropanoic acid (Lactic acid), 2-Methyl 2-hydroxypropanoic acid (Methylactic acid), 2-Hydroxybutanoic acid, 2-Hydroxypentanoic acid, 2-Hydroxyhexanoic acid, 2-Hydroxyheptanoic acid, 2-Hydroxyoctanoic acid, 2-Hydroxynonanoic acid, 2-Hydroxydecanoic acid, 2-Hydroxyundecanoic acid, 2-Hydroxydodecanoic acid (Alpha hydroxylauric acid), 2-Hydroxytridecanoic acid (Alpha hydroxymyristic acid), 2-Hydroxytetradecanoic acid (Alpha hydroxypalmitic acid), 2-Hydroxyoctadecanoic acid (Alpha hydroxystearic acid), 2-Hydroxyeicosanoic acid (Alpha hydroxyarachidonic acid).
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9. A composition according to claim 7 wherein said aralkyl and aryl alpha hydroxyacid is selected from 2-

Phenyl 2-hydroxyethanoic acid (Mandelic acid), 2,2-Diphenyl 2-hydroxyethanoic acid (Benzilic acid), 3-Phenyl 2-hydroxypropanoic acid (Phenyllactic acid), 2-Phenyl 2-methyl 2-hydroxyethanoic acid (Atrolactic acid), 2-(4'-Hydroxyphenyl) 2-hydroxyethanoic acid, 2-(4'-Chlorophenyl) 2-hydroxyethanoic acid, 2-(3'-Hydroxy-4'-methoxyphenyl) 2-hydroxyethanoic acid, 2-(4'-Hydroxy-3'-methoxyphenyl) 2-hydroxyethanoic acid, 3-(2'-Hydroxyphenyl) 2-hydroxypropanoic acid, 3-(4'-Hydroxyphenyl) 2-hydroxypropanoic acid, or 2-(3',4'-Dihydroxyphenyl) 2-hydroxyethanoic acid.

10. A composition according to claim 7 wherein said polyhydroxy alpha hydroxyacid and polycarboxylic alpha hydroxyacid is selected from 2,3-Dihydroxypropanoic acid (Glyceric acid), 2,3,4-Trihydroxybutanoic acid (Isomers; erythronic acid, threonic acid), 2,3,4,5-Tetrahydroxypentanoic acid (Isomers; ribonic acid, arabinonic acid, xylonic acid, lyxonic acid), 2,3,4,5,6-Pentahydroxyhexanoic acid (Isomers; allonic acid, altronic acid, gluconic acid, mannoic acid, gulonic acid, idonic acid galactonic acid, talonic acid), 2,3,4,5,6,7-Hexahydroxyheptanoic acid (Isomers; glucoheptonic acid, galactoheptonic acid etc.), 2-Hydroxypropane-1,3-dioic acid (Tartronic acid), 2-Hydroxybutane-1,4-dioic acid (Malic acid), 2,3-Dihydroxybutane-1,4-dioic acid (Tartaric acid), 2-Hydroxy-2-carboxypentane-1,5-dioic acid (Citric acid), 2,3,4,5-Tetrahydroxyhexane-1,6-dioic acid (Isomers; saccharic acid, mucic acid, etc.), or lactone forms (gluconolactone, galactonolactone, glucuronolactone, galacturonolactone, gulonolactone, ribonolactone, saccharic acid lactone, pantoyllactone, glucoheptonolactone, mannnonolactone, galactoheptonolactone, etc.).

11. A composition according to any preceding claim wherein said alpha ketoacid has the following chemical formula:

(Ra) CO COO (Rb)

wherein Ra and Rb each represent H or an alkyl, aralkyl or aryl group of saturated or unsaturated, isomeric or non-isomeric, straight or branched chain or cyclic form, having 1 to 25 carbon atoms, and in addition Ra may carry F, Cl, Br, I, OH, CHO, COOH or an alkoxy group having 1 to 9 carbon atoms, said alpha ketoacid existing as a free acid or an ester form, or in a salt form with an organic base or an inorganic alkali.

12. A composition according to claim 11 wherein said alpha ketoacid and its ester is selected from 2-Ketoethanoic acid (Glyoxylic acid), Methyl 2-ketoethanoate, 2-Ketopropanoic acid (Pyruvic acid), Methyl 2-ketopropanoate (Methyl pyruvate), Ethyl 2-ketopropanoate (Ethyl pyruvate), Propyl 2-ketopropanoate (Propyl pyruvate), 2-Phenyl-2-ketoethanoic acid (Benzoylformic acid), Methyl 2-phenyl-2-ketoethanoate (Methyl benzoylformate), Ethyl 2-phenyl-2-ketoethanoate (Ethyl benzoylformate), 3-Phenyl-2-ketopropanoic acid (Phenylpyruvic acid), Methyl 3-phenyl-2-ketopropanoate (Methyl phenylpyruvate), Ethyl 3-phenyl-2-ketopropanoate (Ethyl phenylpyruvate), 2-Ketobutanoic acid, 2-Ketopentanoic acid, 2-Ketohexanoic acid, 2-Ketopheptanoic acid, 2-Ketooctanoic acid, 2-Ketododecanoic acid, or Methyl 2-ketooctanoate.

13. A composition according to any preceding claim wherein the said related compound is selected from ascorbic acid, quinic acid, isocitric acid, tropic acid, trethocanic acid, 3-chlorolactic acid, cerebronic acid, citramalic acid, agaricic acid, 2-hydroxynervonic acid, aleuritic acid and pantoic acid.

14. A therapeutic composition for topical treatment of cosmetic conditions or dermatologic disorders comprising dimeric or polymeric forms of hydroxyacids, having the following chemical formula:

$H [-O-C(Ra)(Rb)-CO-]_n OH$

wherein Ra,Rb=H, alkyl, aralkyl or aryl group of saturated or unsaturated, isomeric or non-isomeric, straight or branched chain or cyclic form, having 1 to 25 carbon atoms, and $n=1$ or any numerical number up to 200; Ra and Rb in monomer unit 2, 3, 4 may be the same or the different groups from that in monomer unit 1; the hydrogen atom in Ra and Rb may be substituted by a halogen atom or a radical of lower alkyl, aralkyl, aryl or alkoxy of saturated or unsaturated, isomeric or non-isomeric, straight or branched chain or cyclic form, having 1 to 9 carbon atoms, and the dimeric and polymeric forms of hydroxyacids may be present as a free acid, ester or in a salt form with an organic base or inorganic alkali.

15. A composition according to claim 14 wherein said dimeric or polymeric forms of hydroxyacids are selected from the group consisting of glycolyl glycollate, lactyl lactate, mandelyl mandellate, atrolactyl atrolactate, phenyllactyl phenyllactate, benzilyl benzillate, glycolyl lactate, lactyl glycollate, triglycolic acid, trilactic acid, polyglycolic acid or polylactic acid.

16. A therapeutic composition for topical treatment of cosmetic conditions or dermatologic disorders comprising dimeric or polymeric forms of hydroxyacids, having the following chemical formula:

$[-O-C(Ra)(Rb)-CO-]_n$

wherein Ra,Rb=H, alkyl, aralkyl or aryl group of saturated or unsaturated, isomeric or non-isomeric, straight or branched chain or cyclic form, having 1 to 25 carbon atoms, and $n=1$ or any numerical number, and Ra or Rb may be identical or not identical in the monomer units.

17. A composition according to claim 16 wherein said dimeric or polymeric forms of hydroxyacids are selected from glycolide, lactide, mandelide, atrolactide, phenyllactide, benzilide, methylthylactide, lactoglycolide or glycolactide.

18. A composition according to any one of claims 14 to 17 further comprising a cosmetic or pharmaceutical agent incorporated as an ingredient in said composition.

19. A composition according to any preceding claim for use in the treatment of dry skin, xerosis, ichthyosis, dandruff, brownish spots, keratoses, melasma, lentigines, age spots, liver spots, pigmented spots, wrinkles, blemishes, skin lines, oily skin, acne, warts, eczema, pruritic skin, psoriasis, inflammatory dermatoses, disturbed keratinization, skin changes associated with aging, nail or skin requiring cleansers, conditioning or treatment, and hair or scalp requiring shampooing or conditioning.

20. A therapeutic composition for topical treatment of warts, nail infections, age spots, wrinkles and aging related skin changes comprising at least one member selected from alpha hydroxyacids, alpha ketoacids or related compounds.

21. A composition according to claim 20 wherein said alpha hydroxyacids, alpha ketoacids or related compounds may be present as a free acid, lactone, ester or in salt form with an organic base or an inorganic alkali.

22. A composition according to claim 20 or claim 21 wherein said alpha hydroxyacids, alpha ketoacids or related compounds are selected from 2-hydroxyethanoic acid, 2-hydroxypropanoic acid, 2-methyl 2-hydroxypropanoic acid, 2-phenyl 2-hydroxyethanoic acid, 2,2-diphenyl 2-hydroxyethanoic acid, 2-phenyl 2-methyl 2-hydroxyethanoic acid, 2-phenyl 3-hydroxypropanoic acid, 2-ketopropanoic acid, methyl 2-ketopropionate and ethyl 2-ketopropionate.

23. A cosmetic skin treatment which comprises the topical application to the skin of a composition according to any preceding claim.

24. The use in the preparation of a pharmaceutical or cosmetic composition for the topical treatment of skin conditions, of a combination of an amphoteric or pseudoamphoteric agent and an alpha hydroxyacid, an alpha ketoacid or a related compound.



European
Patent Office

EUROPEAN SEARCH REPORT

Application Number

EP 90 30 8828

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
X	EP-A-0 086 070 (UNILEVER NV) * Page 3, line 35 - page 4, line 20; page 7, lines 12-26 *	1-24	A 61 K 7/48 A 61 K 31/19
X	LU-A-5 814 3 (MEDISAN AB) * Pages 8-9 in the whole (claims 1-8) *	1-24	
A	EP-A-0 273 202 (E.J. VAN SCOTT) -----	1-24	
			TECHNICAL FIELDS SEARCHED (Int. Cl.5)
			A 61 K
The present search report has been drawn up for all claims			

Place of search

The Hague

Date of completion of search

25 October 90

Examiner

BRINKMANN C.

CATEGORY OF CITED DOCUMENTS

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